

ART 19
E30095PCT
Epigenomics AG

Claims (amended)

1. A method for predicting the responsiveness of a subject with a cell proliferative disorder of the breast tissues to a therapy comprising one or more drugs which target the estrogen receptor pathway or are involved in estrogen metabolism, production, or secretion, said method comprising analysing the methylation pattern of one or more target nucleic acids comprising genes taken from the group consisting of STMN1, SFN, S100A2, TGFBR2, TP53, PTGS2, FGFR1, SYK, PITX2, GRIN2D, PSA, CGA, CYP2D6, MSMB, COX7A2L, VTN, PRKCD, ONECUT2, WBP11, CYP2D6, DAG1, ERBB2, S100A2, TFF1, TP53, TMEFF2, ESR1, SYK, RASSF1, PITX2, PSAT1, CGA, and PCAF, and/or their regulatory regions by contacting at least one of said target nucleic acids in a biological sample obtained from said subject prior to or during treatment with one or more agents that convert cytosine bases that are unmethylated at the 5'-position thereof to a base that is detectably dissimilar to cytosine in terms of hybridisation properties.
2. A method according to Claim 1, wherein said genes are selected from the group consisting of TP53, PTGS2, FGFR1, PSA, CGA, CYP2D6, and MSMB.
3. A method according to Claim 1, wherein said genes are selected from the group consisting of STMN1, PITX2, PSA, and CGA.
4. A method according to Claim 1, wherein said genes are selected from the group consisting of STMN1, SFN, S100A2, TGFBR2, SYK, GRIN2D, PSA, COX7A2L, VTN, and PRKCD.
5. A method according to Claim 1, wherein said genes are selected from the group consisting of ONECUT2, WBP11, CYP2D6, DAG1, ERBB2, S100A2, TFF1, TP53, TMEFF2, ESR1, SYK, RASSF1, PITX2, PSAT1, CGA, and PCAF.

ART 19

6. A method according to Claim 1, wherein said genes are selected from the group consisting of TP53, PTGS2, PITX2, CYP2D6, MSMB, WBP11, TMEFF2, ESR1, PITX2, ERBB2, and PCAF.
7. A method according to Claim 1, wherein said genes are selected from the group consisting of TP53, PTGS2, CYP2D6, and MSMB.
8. A method according to Claim 1, wherein said genes are selected from the group consisting of PITX2
9. A method according to Claim 1, wherein said genes are selected from the group consisting of WBP11, TMEFF2, ESR1, PITX2, ERBB2, and PCAF.
10. A method according to Claim 1, wherein said genes are selected from the group consisting of STMN1, SFN, TGFBR2, FGFR1, SYK, GRIN2D, PSA, COX7A2L, VTN, PRKCD, ONECUT2, CYP2D6, DAG1, S100A2, TFF1, TP53, SYK, RASSF1, PSAT1, and CGA.
11. A method according to Claim 1, wherein said genes are selected from the group consisting of FGFR1, PSA, and CGA.
12. A method according to Claim 1, wherein said genes are selected from the group consisting of STMN1, PSA, and CGA.
13. A method according to Claim 1, wherein said genes are selected from the group consisting of STMN1, SFN, S100A2, TGFBR2, SYK, GRIN2D, PSA, COX7A2L, VTN, and PRKCD.
14. A method according to Claim 1, wherein said genes are selected from the group consisting of ONECUT2, CYP2D6, DAG1, S100A2, TFF1, TP53, SYK, RASSF1, PSAT1, and CGA.
15. A method according to Claim 1, wherein said target nucleic acid or acids comprise essentially one or more sequences from the group consisting of SEQ ID NOs: 27, 40,

ART 19
122, 43, 74, 127, 86, 90, 128, 105, 115, 121, 126, 129, 125, 132, 122, 123, 131, 127, 130, 124, and 128, and sequences complementary thereto.

16. A method according to Claim 1, wherein said target nucleic acid or acids comprise essentially one or more sequences from the group consisting of SEQ ID NOs: 68, 50, 74, 90, 91, 92, and 99, and sequences complementary thereto.
17. A method according to Claim 1, wherein said target nucleic acid or acids comprise essentially one or more sequences from the group consisting of SEQ ID NOs: 27, 83, 90, and 91, and sequences complementary thereto.
18. A method according to Claim 1, wherein said target nucleic acid or acids comprise essentially one or more sequences from the group consisting of SEQ ID NOs: 27, 40, 41, 43, 78, 86, 90, 105, 115, and 121, and sequences complementary thereto.
19. A method according to Claim 1, wherein said target nucleic acid or acids comprise essentially one or more sequences from the group consisting of SEQ ID NOs: 126, 137, 129, 125, 132, 122, 123, 131, 133, 134, 127, 130, 135, 124, 128, and 136, and sequences complementary thereto.
20. A method according to Claims 1 to 19, wherein said cell proliferative disorder of the breast tissue is selected from the group consisting of ductal carcinoma *in situ*, lobular carcinoma, colloid carcinoma, tubular carcinoma, medullary carcinoma, metaplastic carcinoma, intraductal carcinoma *in situ*, lobular carcinoma *in situ* and papillary carcinoma *in situ*.
21. A method according to Claims 1 to 20, wherein said subjects are estrogen and/or progesterone receptor positive.
22. A method according to Claims 1 to 5 and 10 to 14, wherein said therapy is for the treatment of a relapse or metastatic cell proliferative disorder of the breast tissues.
23. A method according to Claims 1 to 9, wherein said therapy is an adjuvant treatment.

ART 19

24. A method according to Claim 23, wherein said subjects did not receive a chemotherapeutic treatment.
25. A nucleic acid molecule consisting essentially of a sequence at least 18 bases in length according to one of the sequences taken from the group consisting of SEQ ID NOs: 299, 300, 325, 326, 327, 328, 331, 332, 345, 346, 381, 382, 393, 394, 401, 402, 411, 412, 417, 418, 425, 426, 427, 428, 429, 430, 443, 444, 455, 456, 475, 476, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 573, 574, 599, 600, 601, 602, 605, 606, 619, 620, 655, 656, 667, 668, 675, 676, 685, 686, 691, 692, 699, 700, 701, 702, 703, 704, 717, 718, 729, 730, 749, 750, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, and 794, and sequences complementary thereto.
26. A nucleic acid molecule consisting essentially of a sequence at least 18 bases in length according to one of the sequences taken from the group consisting of SEQ ID NOs: 345, 346, 381, 382, 393, 394, 425, 426, 427, 428, 429, 430, 443, 444, 619, 620, 655, 656, 667, 668, 699, 700, 701, 702, 703, 704, 717, and 718, and sequences complementary thereto.
27. A nucleic acid molecule consisting essentially of a sequence at least 18 bases in length according to one of the sequences taken from the group consisting of SEQ ID NOs: 299, 300, 411, 412, 425, 426, 427, 428, 573, 574, 685, 686, 699, 700, 701, and 702, and sequences complementary thereto.
28. A nucleic acid molecule consisting essentially of a sequence at least 18 bases in length according to one of the sequences taken from the group consisting of SEQ ID NOs: 299, 300, 325, 326, 327, 328, 331, 332, 401, 402, 417, 418, 425, 426, 455, 456, 475, 476, 487, 488, 573, 574, 599, 600, 601, 602, 605, 606, 675, 676, 691, 692, 699, 700, 729, 730, 749, 750, 761, and 762, and sequences complementary thereto.
29. A nucleic acid molecule consisting essentially of a sequence at least 18 bases in length according to one of the sequences taken from the group consisting of SEQ ID NOs:

AAH 19

489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, and 794, and sequences complementary thereto.

30. An oligomer, in particular an oligonucleotide or peptide nucleic acid (PNA)-oligomer, said oligomer consisting essentially of at least one base sequence having a length of at least 10 nucleotides which hybridises to or is identical to one of the nucleic acid sequences according to SEQ ID NO: 299, 300, 325, 326, 327, 328, 331, 332, 345, 346, 381, 382, 393, 394, 401, 402, 411, 412, 417, 418, 425, 426, 427, 428, 429, 430, 443, 444, 455, 456, 475, 476, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 573, 574, 599, 600, 601, 602, 605, 606, 619, 620, 655, 656, 667, 668, 675, 676, 685, 686, 691, 692, 699, 700, 701, 702, 703, 704, 717, 718, 729, 730, 749, 750, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, and 794.

31. An oligomer, in particular an oligonucleotide or peptide nucleic acid (PNA)-oligomer, said oligomer consisting essentially of at least one base sequence having a length of at least 10 nucleotides which hybridises to or is identical to one of the nucleic acid sequences according to SEQ ID NO: 345, 346, 381, 382, 393, 394, 425, 426, 427, 428, 429, 430, 443, 444, 619, 620, 655, 656, 667, 668, 699, 700, 701, 702, 703, 704, 717, and 718.

32. An oligomer, in particular an oligonucleotide or peptide nucleic acid (PNA)-oligomer, said oligomer consisting essentially of at least one base sequence having a length of at least 10 nucleotides which hybridises to or is identical to one of the nucleic acid sequences according to SEQ ID NO: 299, 300, 411, 412, 425, 426, 427, 428, 573, 574, 685, 686, 699, 700, 701, and 702.

33. An oligomer, in particular an oligonucleotide or peptide nucleic acid (PNA)-oligomer, said oligomer consisting essentially of at least one base sequence having a length of at

ART 19

least 10 nucleotides which hybridises to or is identical to one of the nucleic acid sequences according to SEQ ID NO: 299, 300, 325, 326, 327, 328, 331, 332, 401, 402, 417, 418, 425, 426, 455, 456, 475, 476, 487, 488, 573, 574, 599, 600, 601, 602, 605, 606, 675, 676, 691, 692, 699, 700, 729, 730, 749, 750, 761, and 762.

34. An oligomer, in particular an oligonucleotide or peptide nucleic acid (PNA)-oligomer, said oligomer consisting essentially of at least one base sequence having a length of at least 10 nucleotides which hybridises to or is identical to one of the nucleic acid sequences according to SEQ ID NO: 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, and 794.
35. The oligomer as recited in any one of Claims 30 to 34, wherein the base sequence includes at least one CpG dinucleotide.
36. A set of oligomers, comprising at least two oligomers according to any of Claims 30 to 35.
37. A set of oligonucleotides as recited in one of Claims 30 to 36, characterised in that at least one oligonucleotide is bound to a solid phase.
38. A set of at least two oligonucleotides as recited in one of Claims 30 to 36, which is used as primer oligonucleotides for the amplification of nucleic acid sequences comprising one of SEQ ID NO: 299, 300, 325, 326, 327, 328, 331, 332, 345, 346, 381, 382, 393, 394, 401, 402, 411, 412, 417, 418, 425, 426, 427, 428, 429, 430, 443, 444, 455, 456, 475, 476, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 573, 574, 599, 600, 601, 602, 605, 606, 619, 620, 655, 656, 667, 668, 675, 676, 685, 686, 691, 692, 699, 700, 701, 702, 703, 704, 717, 718, 729, 730, 749, 750, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, and 794, and sequences complementary thereto.

ART 19

39. Use of a set of oligonucleotides comprising at least two of the oligomers according to any of Claims 30 to 38 for detecting the cytosine methylation state and/or single nucleotide polymorphisms (SNPs) within the sequences taken from the group SEQ ID NOs: 27, 40, 122, 43, 74, 127, 86, 90, 128, 105, 115, 121, 126, 129, 125, 132, 122, 123, 131, 127, 130, 124, and 128, and sequences complementary thereto.
40. A method for manufacturing an arrangement of different oligomers (array) fixed to a carrier material for predicting the responsiveness of a subject with a cell proliferative disorder of the breast tissues to a therapy comprising one or more drugs which target the estrogen receptor pathway or are involved in estrogen metabolism, production, or secretion by analysis of the methylation state of any of the CpG dinucleotides of the group SEQ ID NOs: 27, 40, 122, 43, 74, 127, 86, 90, 128, 105, 115, 121, 126, 129, 125, 132, 122, 123, 131, 127, 130, 124, and 128, wherein at least one oligomer according to any of the Claims 30 to 35 is coupled to a solid phase.
41. An arrangement of different oligomers (array) obtainable according to Claim 40.
42. An array of different oligonucleotide- and/or PNA-oligomer sequences as recited in Claim 41, characterised in that said oligonucleotides are arranged on a plane solid phase in the form of a rectangular or hexagonal lattice.
43. The array as recited in any of the Claims 41 or 42, characterised in that the solid phase surface is composed of silicon, glass, polystyrene, aluminium, steel, iron, copper, nickel, silver, or gold.
44. A DNA- and/or PNA-array for predicting breast cell proliferative disorders' response to a therapy comprising one or more drugs which target the estrogen receptor pathway or are involved in estrogen metabolism, production, or secretion by analysis of the methylation state of any of the CpG dinucleotides of the group SEQ ID NOs: 27, 40, 122, 43, 74, 127, 86, 90, 128, 105, 115, 121, 126, 129, 125, 132, 122, 123, 131, 127, 130, 124, and 128, comprising at least one nucleic acid according to any of the Claims 30 to 35.

- ART 19
45. A method according to any one of Claims 1 to 24 comprising the following steps:
- a) obtaining a biological sample containing genomic DNA,
 - b) extracting the genomic DNA,
 - c) converting cytosine bases in the genomic DNA sample which are unmethylated at the 5-position, to uracil or another base which is dissimilar to cytosine in terms of base pairing behaviour;
 - d) amplifying at least one fragment of the pretreated genomic DNA, wherein said fragments comprise one or more sequences selected from the group consisting of SEQ ID NO: 299, 300, 325, 326, 327, 328, 331, 332, 345, 346, 381, 382, 393, 394, 401, 402, 411, 412, 417, 418, 425, 426, 427, 428, 429, 430, 443, 444, 455, 456, 475, 476, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 573, 574, 599, 600, 601, 602, 605, 606, 619, 620, 655, 656, 667, 668, 675, 676, 685, 686, 691, 692, 699, 700, 701, 702, 703, 704, 717, 718, 729, 730, 749, 750, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, and 794, and sequences complementary thereto, and
 - e) determining the methylation status of one or more genomic CpG dinucleotides by analysis of the amplificate nucleic acids.
46. The method according to Claim 45, characterised in that Step d) said fragments comprise one or more sequences selected from the group consisting of SEQ ID NO: 345, 346, 381, 382, 393, 394, 425, 426, 427, 428, 429, 430, 443, 444, 619, 620, 655, 656, 667, 668, 699, 700, 701, 702, 703, 704, 717, and 718, and sequences complementary thereto.
47. The method according to Claim 45, characterised in that Step d) said fragments comprise one or more sequences selected from the group consisting of SEQ ID NO: 299, 300, 411, 412, 425, 426, 427, 428, 573, 574, 685, 686, 699, 700, 701, and 702, and sequences complementary thereto.
48. The method according to Claim 45, characterised in that Step d) said fragments comprise one or more sequences selected from the group consisting of SEQ ID NO: 299, 300, 325, 326, 327, 328, 331, 332, 401, 402, 417, 418, 425, 426, 455, 456, 475, 476,

ART 19

487, 488, 573, 574, 599, 600, 601, 602, 605, 606, 675, 676, 691, 692, 699, 700, 729, 730, 749, 750, 761, and 762, and sequences complementary thereto.

49. The method according to Claim 45, characterised in that Step d) said fragments comprise one or more sequences selected from the group consisting of SEQ ID NO: 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, and 794, and sequences complementary thereto.
50. The method according to Claim 45, characterised in that Step e) is carried out by means of hybridisation of at least one oligonucleotide according to SEQ ID NO: 1691 to 1692, 1733 to 1736, 1925-1932, 1941-1954, and 1965 to 2142.
51. The method according to Claim 45, characterised in that Step e) is carried out by means of hybridisation of at least one oligonucleotide according to SEQ ID NO: 2011, 2012, 2017 to 2024, 2031 to 2035, 2035, 2036, 2036, 2037, 2037, 2038, and 2038 to 2044.
52. The method according to Claim 45, characterised in that Step e) is carried out by means of hybridisation of at least one oligonucleotide according to SEQ ID NO: 2003 to 2030.
53. The method according to Claim 45, characterised in that Step e) is carried out by means of hybridisation of at least one oligonucleotide according to SEQ ID NO: 2003 to 2020 and 2045 to 2112.
54. The method according to Claim 45, characterised in that Step e) is carried out by means of hybridisation of at least one oligonucleotide according to SEQ ID NO: 1691 to 1692, 1733 to 1736, 1925 to 1932, 1941 to 1954, 1965 to 2002, 2011 to 2025, 2045 to 2052, 2069 to 2078 and 2127 to 2134.

ART 19

55. The method as recited in Claim 45, characterised in that Step e) is carried out by means of hybridisation of at least one oligonucleotide according to Claims 17 to 21.
56. The method as recited in Claim 45, characterised in that Step e) is carried out by means of hybridisation of at least one oligonucleotide according to Claims 17 to 21 and extension of said hybridised oligonucleotide(s) by means of at least one nucleotide base.
57. The method as recited in Claim 45, characterised in that Step e) is carried out by means of sequencing.
58. The method as recited in Claim 45, characterised in that Step d) is carried out using methylation specific primers.
59. The method as recited in Claim 45, further comprising in step d) the use of at least one nucleic acid molecule or peptide nucleic acid molecule comprising in each case a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NOs: 299, 300, 325, 326, 327, 328, 331, 332, 345, 346, 381, 382, 393, 394, 401, 402, 411, 412, 417, 418, 425, 426, 427, 428, 429, 430, 443, 444, 455, 456, 475, 476, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 573, 574, 599, 600, 601, 602, 605, 606, 619, 620, 655, 656, 667, 668, 675, 676, 685, 686, 691, 692, 699, 700, 701, 702, 703, 704, 717, 718, 729, 730, 749, 750, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, and 794, and complements thereof, wherein said nucleic acid molecule or peptide nucleic acid molecule suppresses amplification of the nucleic acid to which it is hybridized.
60. The method as recited in Claim 45, characterised in that Step e) is carried out by means of a combination of at least two of the methods described in Claims 38 to 42.

:ART 19

61. The method as recited in Claim 45, characterised in that the treatment is carried out by means of a solution of a bisulfite, hydrogen sulfite or disulfite.
62. A method according to any one of Claims 1 to 24 comprising the following steps:
- a) obtaining a biological sample containing genomic DNA,
 - b) extracting the genomic DNA,
 - c) digesting the genomic DNA comprising one or more of the sequences from the group consisting of SEQ ID NOs 27, 40, 122, 43, 74, 127, 86, 90, 128, 105, 115, 121, 126, 129, 125, 132, 122, 123, 131, 127, 130, 124, and 128, and sequences complementary thereto with one or more methylation sensitive restriction enzymes, and
 - d) determining of the DNA fragments generated in the digest of step c).
63. The method according to Claim 62, characterised in that the target sequence or sequences digested in Step c) comprises one or more sequences from the group consisting of SEQ ID NOs 68, 50, 74, 90, 91, 92, and 99.
64. The method according to Claim 62, characterised in that the target sequence or sequences digested in Step c) comprises one or more sequences from the group consisting of SEQ ID NOs 27, 83, 90, and 91.
65. The method according to Claim 62, characterised in that the target sequence or sequences digested in Step c) comprises one or more sequences from the group consisting of SEQ ID NOs 27, 40, 41, 43, 78, 86, 90, 105, 115, and 121.
66. The method according to Claim 62, characterised in that the target sequence or sequences digested in Step c) comprises one or more sequences from the group consisting of SEQ ID NOs 126, 137, 129, 125, 132, 122, 123, 131, 133, 134, 127, 130, 135, 124, 128, and 136.
67. A method according to any one of Claims 62 to 66, wherein the DNA digest is amplified prior to step d).



68. The method as recited in one of Claims 45 to 54 and 67 characterised in that more than six different fragments having a length of 100 - 200 base pairs are amplified.
69. The method as recited in one of Claims 45 to 54 and 68 characterised in that the amplification of several DNA segments is carried out in one reaction vessel.
70. The method as recited in one of the Claims 45 to 54 and 68, characterised in that the polymerase is a heat-resistant DNA polymerase.
71. The method as recited in one of the Claims 45 to 54 and 70, characterised in that the amplification is carried out by means of the polymerase chain reaction (PCR).
72. The method as recited in one of the Claims 45 to 54 and 69 to 70, characterised in that the amplicates carry detectable labels.
73. The method according to Claim 72 wherein said labels are fluorescence labels, radionuclides and/or detachable molecule fragments having a typical mass which can be detected in a mass spectrometer.
74. The method as recited in one of the Claims 45 to 54 and 69 to 73, characterised in that the amplicates or fragments of the amplicates are detected in the mass spectrometer.
75. The method as recited in one of the Claims 74 and/or 73, characterised in that the produced fragments have a single positive or negative net charge for better detectability in the mass spectrometer.
76. The method as recited in one of Claims 73 to 75, characterised in that detection is carried out and visualised by means of matrix assisted laser desorption/ionisation mass spectrometry (MALDI) or using electron spray mass spectrometry (ESI).
77. The method as recited in one of the Claims 45 to 76, characterised in that the genomic DNA is obtained from cells or cellular components which contain DNA, sources of DNA comprising, for example, cell lines, histological slides, biopsies, tissue embed-

ART 19
ded in paraffin, breast tissues, blood, plasma, lymphatic fluid, lymphatic tissue, duct cells, ductal lavage fluid, nipple aspiration fluid, bone marrow and combinations thereof.

78. A kit comprising a bisulfite (= disulfite, hydrogen sulfite) reagent as well as oligonucleotides and/or PNA-oligomers according to one of the Claims 30 to 38.
79. A kit according to Claim 78, further comprising standard reagents for performing a methylation assay from the group consisting of MS-SNuPE, MSP, Methyl light, Heavy Methyl, nucleic acid sequencing and combinations thereof.
80. The use of a method according to one of Claims 1 to 24, 45 to 77, a nucleic acid according to Claims 25 to 29, of an oligonucleotide or PNA-oligomer according to one of the Claims 30 to 35, of a kit according to Claim 78 or 79, of an array according to one of the Claims 40 to 44, a method of manufacturing an array according to Claim 39 or of a set of oligonucleotides according to one of Claims 36 to 38 for the treatment, characterisation, classification and/or differentiation, of breast cell proliferative disorders.